REMARKS/ARGUMENTS

With this amendment, claims 1-28 are pending. Claims 2-8 are withdrawn. Claims 9, 16, 23-25 and 29 are cancelled without prejudice. For convenience, the Examiner's rejections are addressed in the order presented in a November 27, 2007, Office Action.

I. Rejections under 35 U.S.C. §112, first paragraph, written description

The Examiner rejected claims 1, 12, 13, 15, 17-19, and 22 under the written description requirement of 35 USC § 112, first paragraph. The Office Action alleged that the specification does not disclose the complete or partial structure or chemical/ physical properties of the claimed genus or describe how to obtain specific peptides that would be effective at treating multiple sclerosis (MS).

To the extent the rejection applies to the amended claims, Applicants respectfully traverse. As currently applied, the specification does comply with U.S. patent law for description of an amino acid sequence. The Federal Circuit court of Appeals has addressed the level of description adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. See, *e.g.*, *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). As alluded to by the Examiner, an applicant may show that an invention is complete by

> . . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Id.* at 1613.

Applicants disclose that the core sequence of ANDF III (SEQ ID NO:2) is minimally required to treat MS. As stated in paragraph [0051], additional amino acids can be added to both the N-terminus and C-terminus of the active peptide without loss of biological activity. Thus, at least the partial structure of the polypeptide genus of the claims is provided by the core ADNF sequences. At a minimum, the core ADNF III sequence is correlated with lessening of MS symptoms (*i.e.*, a biological function), as demonstrated in the Example at

paragraphs [101] through [106]. Applicants have also provided methods to obtain the polypeptides of the claimed genus, for example, using conventional peptide synthesis or recombinant techniques (see paragraphs [0087] through [0094]).

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *See, e.g.,* 66 Fed. Reg. 1099, 1106 (2001). In *Falkner v. Inglis*, the Federal Circuit ruled that, for claims to nucleic acid sequences, and by analogy to amino acid sequences, absence of examples does not render written description inadequate and that actual reduction to practice is not required. *See, e.g., Id.* at 1008.

While claim 1, for example, describes a large number of possible peptide sequences, a skilled artisan would recognize that each of the sequences includes a functional core ADNF III peptide and be able to add additional amino acids as described. The specification provides examples of peptides within the scope of claim 5 (*e.g.*, SEQ ID NOs:2 and 9-12), as well as examples of peptides that may be added to either side of the ADNF core sequence (*e.g.*, paragraph [0049]). Paragraphs [0062] and [0063] disclose other such sequences, where the amino acids added to the core peptide comprise a membrane translocation domain, a peptide with additional functional qualities. The description therefore provides a representative number of exemplary species and presents the possibility of adding functionality to the core ADNF peptide. A skilled artisan would not require the disclosure of each additional polypeptide species within the genus of the claims to recognize that the Applicants had possession of the invention, *i.e.*, MS treatment with a polypeptide comprising a core ADNF III peptide.

The specification describes the ADNF III core amino acid sequence that is required to treat MS (*i.e.*, SEQ ID NO:2) and provides several examples of proteins with additional amino acids (*i.e.*, SEQ ID NOs:9-12). A person with skill in the art would recognize that the inventors had possession of the invention, *i.e.*, treating MS with a polypeptide comprising a core ADNF III peptide, at the time of filing. The claims are therefore in compliance with the written description requirement of 35 USC § 112, first paragraph, and Applicants respectfully request withdrawal of the rejection under that section.

II. Rejections under 35 U.S.C. §103(a)

Claims 1, 10-15, 17-22, and 26-28 are rejected as allegedly obvious by either WO 98/35042 or by US Patent No. 6,613,740 (Gozes *et al.*) in view of either US2002/001301 (Brenneman *et al.*) or Voet *et al.* and Goodman *et al.* To the extent the rejections apply to the amended claims, Applicants respectfully traverse the rejections.

To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. MPEP§2143. See also *In re Rouffet,* 47 USPQ2d 1453. The court in *Rouffet* stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination." *Rouffet* at 1459. The court has also stated that actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (1999). Under the standards listed above, the Office Action does not establish a prima facie case of obviousness.

A. WO 98/35042 or Gozes et al. in view of Brenneman et al.

Claims 1, 10, 11, 14, 15, 17,20-22, and 26-28 are rejected under 35 U.S.C. §103(a) WO 98/35042 or Gozes *et al.* in view of Brenneman *et al.* According to the Office Action both Gozes *et al.* and WO 98/35042 teach methods of using ADNF III polypeptides for treatment and prevention of neurological difficulties; Brenneman *et al.* allegedly teaches administration of ADNF polypeptides or nucleic acids by recited means to treat conditions related to increased neuronal cell death. According to the Office Action, based on the teachings of the cited references, those of skill would have reasonably expected success in treating an autoimmune disease using an ADNF III polypeptide. Applicants respectfully disagree.

The arguments presented by the Office Action appear to assert that the claimed species of diseases treated with ADNF III polypeptides are part of a genus of treatable diseases

listed in the cited references. However, none of the cited references, Gozes *et al.*, WO 98/35042, or Brenneman *et al.* specifically call out the claimed species, *i.e.*, treatment of multiple sclerosis. The Office Action fails to demonstrate that one of skill would go beyond the listed diseases to arrive at multiple sclerosis.

The cited references disclose and demonstrate prevention of neuronal cell death after administration of ADNF III proteins. In contrast, using a mouse model for multiple sclerosis, the specification provides evidence that administration of ADNF III protein inhibits proliferation of immune cells. *See, e.g.*, specification at page 31, lines 5-11 and new claim 29. The cited references provide no teachings that would lead those of skill to predict that administration of ADNF III would have an effect on immune cell proliferation and thus would be useful to treat autoimmune diseases, including multiple sclerosis.

B. WO 98/35042 or Gozes et al. in view of Voet et al. and Goodman et al.

Claims 1, 10-15, 17-22, and 26-28 are rejected as allegedly obvious by either WO 98/35042 or by Gozes *et al.* in view of Voet *et al.* and Goodman *et al.* The alleged disclosures of WO 98/35042 and Gozes *et al.* are provided above. Voet *et al.* and Goodman *et al.* provide general teaching on the advantages of peptides comprising D-amino acids. Neither Voet *et al.* nor Goodman *et al.* provide teachings regarding treatment of any disease using ADNF III polypeptides, including autoimmune diseases, *e.g.*, multiple sclerosis. Thus, Voet *et al.* and Goodman *et al.* cannot overcome the deficiencies of WO 98/35042 or Gozes *et al.* listed above. This group of cited references also fails to render predictable inhibition of immune cell proliferation by administration of ADNF III polypeptides.

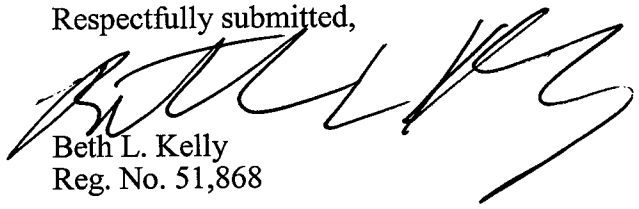
In view of the above amendments and remarks, withdrawal of the rejections for alleged obviousness is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,



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